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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,125	05/22/2001	Elizabeth S. Light	112/002/CON1	9583

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/863,125	Light
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 21, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *27-30* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *27-30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 21, 2003 has been entered.

Specification

2. Claim 27 has been amended.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-30 are rejected over the recitation of the phrase, "conventional" in claim 27. In absence of the definition of the term "conventional" either in the specification or in the claim, it is

not clear what range of microscopic conditions are claimed. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 27-30 are rejected under 35 U.S.C. 103(a) over Lizard et al. (Histochemistry, (1994), Vol. 101, pages 303-310) in view of Bargmann et al. (U.S. Patent 4,935,341) (June 19, 1990) further in view of MacAulay (U.S. Patent 6,483,641 B1) (November 19, 2002).

This rejection is based on the fact that any microscopic method can be considered as "conventional" in absence of any definition of the term in the specification or the claim. Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, any brightfield microscopic method under any suitable conditions can be used for visual detection of a gene in chromosomal DNA. Lizard et

al teach a method of visually detecting a single copy of the gene in chromosomal DNA in an intact cell using brightfield microscopy (Abstract), comprising:

heating the tissue or cell sample sufficiently to dissociate the native chromosomal target strands of DNA (Materials and Methods Section, Page 304, Column 2):

contacting the tissue or cell sample with a detectably-labeled nucleic acid probe under conditions that allow the rehybridization of the labeled nucleic acid to form a target-probe duplex (Materials and Methods Section);

contacting the target-probe duplex with an anti-label antibody under conditions allowing the antibody to bind to the label (Materials and Methods Section);

contacting the anti-label antibody with an enzyme and a chromogen composition under conditions allowing the development of a visually detectable chromogen substrate signal at each target-probe duplex separate and distinct from the chromogenic signals of other copies of the chromosomal target nucleic acid sequence (Materials and Methods Section); and

detecting the chromogenic substrate signal using brightfield microscope conditions (Abstract, Materials and Methods Section, Microscopic examination Subsection, and Figures 1-4).

Lizard et al teach a method, wherein the detectably-labeled nucleic acid probe is labeled with a moiety selected from biotin (Abstract and Materials and Methods Section).

Lizard et al teach a method, wherein the enzyme is selected from phosphatase and a peroxidase (Materials and Methods Section, FISH, EISH, and detection of DNA-DNA hybrids Subsection).

Lizard et al teach a method, wherein the chromogen is selected from NBT/BCIP (Materials and Methods Section, FISH, EISH, and detection of DNA-DNA hybrids Subsection).

Lizard et al do not teach the method, wherein the Her-2/neu gene is detected by its specific corresponding probe.

Bargmann et al. teach the method, wherein the Her-2/neu gene is detected by its specific corresponding probe. (Abstract and Column 2, line 1 to Column 5, line 20).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the Her-2/neu gene is detected by its specific corresponding probe. of Bargmann et al. in the detection of nucleic acids in cells by chromogenic method of Lizard et al. since Bargmann et al. state, " The approach described above has been used successfully in identifying the point mutation which causes activation of the neu protooncogene in DNA from a chemically induced rat neuroblastoma. It has also been used to verify the occurrence of the same activating point mutations, suspected to be present in, in seven other neu oncogenes. The approach described can be used, with modification, in identifying point mutations which cause activation of human neu oncogenes (Column 4, lines 13-23)". By using these strong motivations as well as scientific reasoning, one ordinary practitioner would have combined and substituted the method, wherein the Her-2/neu gene is

detected by its specific corresponding probe. of Bargmann et al. in the detection of nucleic acids in cells by chromogenic method of Lizard et al. to improve the detection and localization of specific oncogene nucleic acid sequences within morphologically intact cells. An ordinary practitioner would have been motivated to combine and substitute the method, wherein the Her-2/neu gene is detected by its specific corresponding probe. of Bargmann et al. in the detection of nucleic acids in cells by chromogenic method of Lizard et al.. in order to achieve the express advantage, as noted by Bargmann et al, of the method which provides the approach that can be used successfully in identifying the point mutation which causes activation of the neu protooncogene in DNA from a chemically induced rat neuroblastoma and which also can be used to verify the occurrence of the same activating point mutations, suspected to be present in seven other neu oncogenes and which further can be used, with modification, in identifying point mutations which cause activation of human neu oncogenes.

Lizard et al. in view of Bargmann et al do not teach the visual detection using conventional brightfield microscope conditions.

MacAulay teaches the visual detection using conventional brightfield microscope conditions (Abstract and Column 22, line 58 to Column 23, line 12 and Figures 1-14 and claims 1-62).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method of the visual detection using conventional brightfield microscope conditions of MacAulay in the detection of nucleic acids in

cells by chromogenic method of Lizard et al in view of Bargmann et al since MacAulay states, " This allows for a more accurate quantitation of the amount of light lost by absorption. This can be particularly important when attempting to quantitate the total amount of light that is absorbed over given areas of the sample and will provide a more precise spatial absorption representation of the sample (Column 23, lines 7-12)". By using these strong motivations as well as scientific reasoning, one ordinary practitioner would have combined and substituted the method of the visual detection using conventional brightfield microscope conditions of MacAulay in the detection of nucleic acids in cells by chromogenic method of Lizard et al in view of Bargmann et al. to improve the detection and localization of specific oncogene nucleic acid sequences within morphologically intact cells. An ordinary practitioner would have been motivated to combine and substitute the method of the visual detection using conventional brightfield microscope conditions of MacAulay in the detection of nucleic acids in cells by chromogenic method of Lizard et al in view of Bargmann et al . in order to achieve the express advantage, as noted by MacAulay, of the method which allows for a more accurate quantitation of the amount of light lost by absorption and which can be particularly important when attempting to quantitate the total amount of light that is absorbed over given areas of the sample and provides a more precise spatial absorption representation of the sample.

Response to Amendment

7. In response to amendment, previous 103(a) rejections is hereby withdrawn. However, new 112 (second paragraph) and 103(a) rejections have been included.

Response to Arguments

8. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)308-1119. Any inquiry of general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703)605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 is (703) 746-4979. Please note that the faxing of such papers must conform with the Notice to comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

Patent Examiner

Art Unit 1634

June 20, 2003